Associations between weight change over 8 years and baseline body mass index in a cohort of continuing and quitting smokers

Lycett, D. , Munafò, M. , Johnstone, E. , Murphy, M and Aveyard, P.

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ASSOCIATIONS BETWEEN WEIGHT CHANGE OVER EIGHT YEARS AND BASELINE BODY MASS INDEX IN A COHORT OF CONTINUING AND QUITTING SMOKERS

Authors

Deborah Lycett[1]

Marcus Munafò[2]

Elaine Johnstone[3]

Michael Murphy[4]

Paul Aveyard[1]

Affiliations:

1 UK Centre for Tobacco Control Studies, Primary Care Clinical Sciences, University of Birmingham, UK.

2 Department of Experimental Psychology, University of Bristol, Bristol, UK.

3 Department of Clinical Pharmacology, University of Oxford, UK.

4 Childhood Cancer Research Group, University of Oxford, UK.

Corresponding Author:

Deborah Lycett, Primary Care Clinical Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, d.lycett@bham.ac.uk, Tel: 0121 414 3765 Fax: 0121 414 6571

Conflicts of Interest

Paul Aveyard has done consultancy work on smoking cessation for Pfizer, McNeil, and Xenova Biotechnology. Marcus Munafò has received fees for invited lectures from the

National Health Service, GlaxoSmithKline, Novartis, the Moffitt Cancer Research Center and the Karolinska Instituet, and received benefits in kind (hospitality etc.) from various pharmaceutical companies. He has received research and travel support from the European Research Advisory Board, GlaxoSmithKline, Pfizer Consumer Healthcare and Novartis. Consultancy has been provided to the European Commission, The American Institutes for Research, the National Audit Office and G-Nostics Ltd. Elaine Johnstone has received consultancy income from European Network for Smoking Prevention. Michael Murphy has received consultancy income from the European Network for Smoking Prevention and has provided scientific consultancy services through the University of Oxford ISIS Innovation to the National Audit Office and G-Nostics Ltd.

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ABSTRACT

Aim

To examine the association between weight change and baseline body mass index(BMI) over 8 years in a cohort of continuing and quitting smokers.

Design

Prospective cohort.

Setting

Oxfordshire general practices nicotine patch/ placebo trial with 8 year follow-up.

Participants:

85 participants were biochemically proven abstinent at 3, 6, 12 months and 8 years (abstainers). 613 smoked throughout the 8 years (smokers), 26 quit for a whole year but were smoking again by 8 years (relapsed). 116 smoked for the first year but were abstinent at 8 years (late abstainers).

Measurements:

Weight and BMI was measured at baseline and at 8 years. Regression models were used to examine weight gain by smoking status and the association of BMI at the time of quitting.

Findings:

Abstainers gained 8.79kg, (SD 6.36), [95%CI 7.42, 10.17]. Smokers gained 2.24kg (6.65) [1.7, 2.77]. Relapsed smokers gained 3.28kg (7.16) [0.328, 6.24]. Late abstainers gained 8.33kg (8.04) [CI 6.85, 9.81]. The association between baseline BMI and weight change was modified by smoking status. In smokers there was a negative linear association of BMI, while in abstainers, a J-shaped curve fitted best. These models estimated weight change over 8 years in abstainers of +9.8kg, +7.8kg, +10.2kg, +19.4kg and in smokers of +3.9kg, +2.6kg, 1.0kg and -0.8kg where BMI was 18, 23, 29 and 36 respectively.

Conclusion:

Obese smokers gain most weight on quitting smoking, while obese continuing smokers are likely to remain stable or lose weight. Obese quitters have the greatest need for interventions to ameliorate weight gain.

INTRODUCTION

Weight gain is a well known consequence of smoking cessation.[1,2] It may deter smokers from attempting to quit [3] and offsets some advantages of giving up smoking. Smoking cessation-related weight gain partly explains the finding that the incidence of type II diabetes is increased by 50-100% in the years after cessation[4, 5] and there is a 30% increased risk of hypertension compared to continuing smoking.[6] The improvement in lung function of quitters decreased by 38% in men and 17% in women as a consequence of weight gain.[7]

There are few studies providing long-term follow up of smokers and quitters to examine changes in body weight. Most are population-based studies, where smoking status is typically characterised as point prevalence abstinence and where the date of quitting is uncertain, usually lying between follow up occasions.[1] Using point prevalence abstinence underestimates weight gain.[2] The first aim of this study was to examine weight gain over eight years in a group with well-characterised smoking status.

Reviews have examined characteristics associated with greater weight gain and there are conflicting findings on the association between body mass index (BMI) at the time of

quitting and weight gain.[1,8,9] One study showed higher baseline BMI was positively associated with subsequent weight gain. Three showed higher BMI was negatively associated with weight gain, and four found no association. No study investigated whether there was a curvilinear relationship of BMI and post cessation weight gain. The second aim was therefore to examine more fully the relationship of baseline BMI to change in weight in those who quit or continued to smoke.

METHODS

Participants

1686 participants, aged between 25 and 65 years, smoking 15 or more cigarettes a day enrolled in a clinical trial of a 21mg nicotine patch or placebo in 19 general practices in Oxfordshire, UK, between June 1991 and March 1992. They were invited to take part in a stop smoking study through a letter from their general practitioner (GP). They made an appointment with a nurse who told them what the study involved and then they saw their GP one week later, this was when they were recruited, they were expected to quit completely from this day and given patches.[10] The patch was used for 3 months then stopped and participants were reviewed at 4, 8 and 12 weeks. Participants were followed up 6 and 12 months later.[11] Abstinence was confirmed by expired CO<10ppm when participants were using the nicotine patch and by salivary cotinine <20ng/ml after they had stopped using the patch. Cotinine is considered a more reliable measure of abstinence but, as it is a metabolite of nicotine, it cannot confirm abstinence during nicotine replacement therapy.[10] An unplanned follow up took place eight years later, 1625 participants were living, we were able to trace and contact 1532 participants, 840 of these responded. Baseline body mass index (BMI) was similar between responders and non-responders.

However, responders were older (43.0 vs 41.5 years p=0.010), more likely to be female (59% v 52% P<0.005) and have stopped smoking during the trial than non-responders (13% v 6% P<0.0001 quit for 1 year). Ethical approval for this was granted by Anglia and Oxford Multicentre Research Ethics Committee, and 86 local research ethics committees.[12]

Height and weight were measured at trial entry, although this was self-reported in 19% of participants. At eight year follow up, weight was self-reported as the questionnaire was completed by post. Participants completed questionnaires on smoking history and quit attempts that spanned the last 8 years and smoking status was confirmed by salivary cotinine. If no sample was supplied (9%) participants were considered to be smoking.

Abstainers were defined as having stopped smoking on or around quit day and declared continuous total abstinence from three months to a year and were still abstinent eight years later. Abstinence was biochemically verified at 3, 6, 12 months, and 8 years. Ninety eight percent of abstainers were continuously abstinent between one and eight years, but 2% reported relapsing after one year but then quit again prior to eight-year follow up. Smokers were defined as those who were smoking at 8 year follow up and were smoking at every intervening follow up. People not attending follow up in the first year were considered as smokers. Relapsers were those who were biochemically confirmed abstinent at 3, 6, and 12 months but relapsed by 8 years. Late abstainers were those who smoking during the first year but were confirmed abstinent at 8 years.

Statistical Methods

All statistical tests were carried out using Statistical Package for Social Sciences version 15 for windows software (SPSS 15.0). The characteristics of each of the four groups defined by smoking status were summarised with means and SDs or proportions. Chi squared tests and one-way ANOVA with Games-Howell post hoc testing were used to identify differences between the groups. Differences were taken into account in multivariate regression analysis (see below). Means, SDs and 95% confidence intervals (95% CI), were calculated for weight change within each smoking status. We compared self reported weight and BMI data with measured weight and BMI data.

We calculated the percentage of quitters that gained more weight than the average continuing smoker. We compared the proportion of smokers that were in each of the groups defined by the World Health Organisation (WHO) categories of BMI (defined in the Web appendix) at baseline and at eight years using Mann-Whitney-U tests.

Linear regression analysis was used to investigate the differences in weight change (from baseline to 8 year follow-up) according to the four groups defined by smoking status. This was adjusted for potential confounders using multiple linear regression. Potential confounders were identified from the reviews on predictors of post cessation weight gain weight gain.[1,8] Categorical variables (treatment allocation, gender, ethnic group (white European/non-white European) , and socio-economic status measured by the Registrar General's classification of occupational status[13] were recoded into dummy variables. Continuous variables (BMI, height, age, number cigarettes/day, cigarette dependence measured by the Horn Russell (HR) score[14], and weekly units of alcohol consumed at baseline (1 unit defined as 8g of ethanol) were centred around the mean. These were

entered stepwise and considered potentially important if the association between them and the outcome had a p value of <0.2.[15]

To investigate whether the effect of BMI depended upon smoking status linear regression was carried out in the combined sample of smokers and abstainers. Terms indicating smoking status, baseline BMI in kg/m^2 and a multiplicative interaction term between the two were included. Potential confounders were added as above.

There was evidence that smoking status modified the effect of BMI on weight change and so separate models for abstainers and smokers examined these relationships further. In both models, we examined for curvilinear relations between BMI and weight change by sequentially adding linear, quadratic, and cubic terms for BMI. Ninety five percent prediction intervals were calculated from the best fitting models to estimate the likely weight gain of most abstainers or smokers. In sensitivity analysis, the analysis was repeated including relapsed smokers within the smokers group and late abstainers within the abstainers group. Outliers defined by extreme baseline BMI and extreme weight change were removed and the models re-run to examine whether the coefficients changed.

RESULTS

Baseline characteristics

Baseline characteristics of the smoking status groups differed modestly and significantly in age, treatment allocation, and Horn Russell Score ($p<0.05$) (Table 1, Web appendix). Baseline weight data did not differ much or significantly between those whose weight was

measured and those who self-reported. A t-test showed a mean difference of -0.58kg (-2.91, 1.75).

Weight change

Weight change in those who self reported at both points in time did not differ significantly from those who were measured at baseline and self reported at 8 years. The mean difference (95% confidence interval) was -0.40kg (-1.67, 0.87). There was no significant difference between measured or self-reported baseline BMI. The mean difference was 0.47kg/m^2 (-0.15, 1.09). Eighty three percent of quitters gained more weight than the average smoker (Figure 1. Web Appendix). Over the eight years, 15% of quitters became obese compared to 2% of smokers, while 18% of quitters became overweight compared to 5% of smokers (Figure 2. Web Appendix).

Mean weight and BMI change according to smoking status

Abstainers gained 8.79kg (SD 6.36) and BMI increased by 3.26kg/m^2 (SD 2.94). This was 6.55kg more than smokers; who gained on average 2.24kg (SD 6.65) in weight and a 0.94kg/m^2 (SD 2.92) in BMI. Late abstainers, who were not continuously abstinent during the first year but quit before 8 years had a mean weight gain of 8.33kg (SD 8.84), and this was not significantly different to those who had been quit from the end of treatment. Those who had quit smoking for the whole of the first year and subsequently relapsed gained a mean of 3.28kg (SD 7.16); this was not significantly different to smokers. Adjustment for potential confounders did not change these estimates (Table 2).

Table 2 here

Weight Change and Baseline BMI

This analysis was conducted on smokers and abstainers only for simplicity (excluding late abstainers and relapsers). There was evidence that the association between BMI and weight change was modified by smoking status, with a p value for the interaction term being 0.002 both with and without adjustment for potential confounders. Accordingly, separate regression models in abstainers and continuous smokers were examined.

Association between BMI and weight change in abstainers

Regression modelling showed a significant linear association between BMI and weight gain in abstainers. Adding a quadratic term improved the fit (p for R^2 change = 0.015), but the cubic term did not improve this further. The quadratic model accounted for 11% of the variability in weight change (Figure 3) and the coefficients changed only slightly on adjustment for potential confounders (Table 3). This model estimated mean weight change over 8 years in abstainers of +9.8kg, +7.8kg, +10.2kg, +19.4kg where BMI was 18, 23, 29 and 36 respectively (Table 5).

Table 3 here
Figure 3 here

Association between BMI and weight change in smokers

There was a significant, negative, linear association between BMI and weight change in smokers ($p<0.001$) and the fit was not improved by adding higher order terms (Figure 3). The negative association remained largely unchanged when adjusted for confounders

(p=0.002), (Table 4). This model estimated mean weight change smokers of +3.9kg, +2.6kg, 1.0kg and -0.8kg where BMI was 18, 23, 29 and 36 respectively (Table 5).

Table 4 here

Sensitivity Analysis

Late abstainers were added to the abstainers who had been abstinent for the entire 8 years while relapsers were added to the smokers who had smoked for the entire 8 years. The regression models on these combined groups gave similar models and estimates to those derived from the smokers and abstainers only (Table 5).

Excluding participants with higher baseline BMIs, extreme weight gain, and excluding outliers judged by visual inspection of a plot did not really change the findings (Table 5).

Table 5 here

Estimating weight change in individuals

Although the estimates for mean weight change differed according to BMI, there was overlap in the estimates for individuals. Calculating 95% prediction intervals in abstainers using the quadratic model gave values of -3 and 22kg for a BMI of 18, -4 and 20kg for a BMI of 23 and -2 and 22kg for a BMI of 29 and 5 and 33kg for a BMI of 36.

Calculating 95% prediction intervals in smokers using the linear model gave values of -9kg and 17kg for a BMI of 18, -10kg and 16kg for a BMI of 23, -12kg and 14kg for a BMI of 29 and -14kg and 12kg for a BMI of 33.

DISCUSSION

In a cohort of people trying to stop smoking, those who failed and continued smoking for eight years gained about 2kg. Those who abstained from smoking for eight years gained nearly 9kg. People who stopped smoking for a whole year but then resumed smoking had a weight gain that was similar to and not significantly different from continuous smokers. Some quitters gained much more than average, with those who were underweight or overweight on cessation being most likely to gain most. Only a quarter of long-term abstainers were of healthy weight after eight years. The findings were robust to sensitivity analyses.

Strengths and limitations of this study

In a cohort of smokers followed for eight years, many smokers will try to quit and many quitters relapse. In this study, only two abstainers relapsed after a whole year of abstinence, something consistent with other long-term follow up studies.[16] All abstainers were biochemically verified as abstinent four times over the 8 year follow up. Likewise although some smokers tried to quit, they were smoking at each follow up point. The strength of this study therefore lies in its accurate characterisation of both these groups, which leads to more precise estimates of weight change. There is evidence that weight gain on cessation is under-estimated when smoking status is measured by point prevalence or by self-report because self-reported point prevalence will classify intermittent smokers and recent quitters as abstinent.[1,2] The cohorts of late abstainers and relapsers are less well characterised as the time of individuals quitting and relapsing is variable, these events could occur at any time after year 1 and before year 8. However, these groups showed similar estimates of weight change and weight change in relation to baseline BMI, indicating that

for most their relapsed or quit state was sufficiently well established for weight change to reflect that of long term quitters and smokers. In support of this other studies have shown that the greatest weight change associated with smoking status occurs rapidly.[27]

This study is limited by use of self-reported weight and BMI data at 8 year follow-up. However, sensitivity analysis showed no differences in mean baseline weight, BMI or weight change when measured and self-reported data was compared. The validity of self-reported weight data has also been demonstrated in other epidemiological studies,[17] suggesting that reporting bias is not a likely explanation of our results. In particular, to explain the J-shaped curve in abstainers would require a pattern of misreporting weight that varied by baseline BMI such that people with a low or a high BMI eight years previously would over estimate their current weight or people with an ideal BMI eight years ago would underestimate their current weight. This seems unlikely.

Only 52% of the living participants enrolled in the original trial responded at 8 year follow up, with success at quitting in the trial being the factor most strongly associated with response. However, non response is an unlikely explanation of our findings and it is reassuring that baseline weight and BMI did not differ between responders and non responders. The study participants enrolled in a smoking cessation study and responded to a questionnaire on smoking status at follow up, with only a single question on weight. It is unlikely therefore that whether individuals gained weight or their pattern of weight change in relation to BMI was associated with failure to respond. For non-response to explain the association between BMI and weight change, weight change in non responders would have to have been the reverse of what we observed in responders. That is among non-

responding quitters weight gain would have resulted in an inverted-J shaped relation with baseline BMI, with those of a healthy BMI gaining the most weight. There is no plausible reason for such an association.

Our cohort did not contain never-smokers so we have been unable to compare weight change in smokers and quitters to never smokers. However data from other cohorts allows some comparison which helps us to consider the impact this weight gain has on the population's weight as a whole. The OXCHECK cohort[18] and the Caerphilly male cohort[19] show weight gain in quitters during the first 5 years after stopping is greater than in never smokers. Cross sectional analysis of these cohorts show never smokers and ex-smokers have a similar BMI. However the vast majority of cross sectional studies show the BMI of ex-smokers exceeds that of never smokers, suggesting that post-cessation weight gain has public health importance .[1,20]

Our cohort included predominately white European people living in Oxfordshire, UK. There is evidence that weight gain varies by ethnic group. For example, African Americans have greater weight after stopping smoking than European Americans [21,22]. It is therefore possible that other ethnic groups might have a different pattern of weight gain in relation to BMI than we observed in this cohort.

Comparison with other literature

We know of only two other prospective studies that have reported on weight gain over the long-term in biochemically confirmed abstainers. The Lung Health Study found abstainers gained 8.2kg over 5 years whereas smokers gained 1.6kg, a difference of 6.6kg,[27] almost

identical to that we reported here. A smaller study of 45 abstainers showed a mean weight gain of 8.9kg over 4 years but did not report weight change for continuing smokers.[28]

Weight gain in a quit attempt is reduced by about 0.5kg whilst on NRT patches, but there is no evidence that it is permanently prevented.[29] In this trial, NRT was used for 12 weeks only and no long-term abstainers were using NRT at follow up. Previous analysis on these data showed no effect of NRT use on weight gain at eight years.[30]

No other studies have investigated a curvilinear relationship of weight gain according to BMI, although some studies have hinted that such a relationship might exist. Froom *et al* reported weight gain was lowest in those with a between BMI 25.8-27.7 and higher in those with a BMI above or below these values.[31] Caan *et al* found that lighter and heavier women gained more weight than those of intermediate weight, but this pattern was not seen after adjusting for confounders.[25] Other studies have reported no association with baseline BMI,[26,32] some have found a negative linear association,[33,34,35] and some a positive linear association.[36,37] This may be explained because these studies modelled a linear relationship between BMI and weight gain. A linear model would tend to show no association or a weak positive linear association if the true association was U- or J-shaped. Re-evaluating data from the Lung Health Study and the Caerphilly cohort using polynomial modelling would be useful to confirm or refute our results.

Implications for clinical practice

Patients in a smoking cessation clinic want to know how much weight they might gain on cessation. The mean and 95% confidence intervals give information about average or

population effects, but do not give individuals a range in which their weight is likely to lie. These are better defined by prediction intervals. Our models showed that someone with a BMI of 22 who quits smoking and maintains abstinence can expect to lose up to 2kg or gain up to 20kg. However, at higher BMIs, the prediction intervals were more useful with a 95% chance that someone with a BMI of 36 would gain between 5kg and 33kg. The 95% prediction intervals were wide, therefore, and the variables we measured, typical of those obtained in a smoking cessation clinic, explained only about 17% of the variability in weight gain in quitters. We did not measure changes in metabolic rate, energy intake or physical activity, all of which are known to influence weight gain after stopping smoking.(23,24,25,26)

Implications for research

If the association between BMI and weight gain on cessation is causal, we would need to delineate behavioural or physiological mechanisms. Nicotine suppresses appetite and increases metabolic rate.[23] Underweight smokers might gain more weight than ideal weight smokers because they are particularly susceptible to these effects and, when they are removed by stopping smoking, greater weight gain results. Those who are already obese while smoking may have a cluster of unhealthy behaviours if, for example, they also eat a high fat diet, this may be accentuated without nicotine to restrain their appetite. This may result from an increased appetite for sweet and fatty food.[25] Alternatively those who are obese while smoking might be those who are genetically predisposed to obesity, perhaps through poor expression of appetite regulatory hormones[38,39] and, once the appetite suppressing effect of nicotine is removed, weight increases more than healthy weight counterparts.

Conclusions

Smokers who quit smoking gain 6-7kg more than if they had continued smoking, while those who quit for a substantial period and then resume smoking seem to resume their 'smoking weight'. This study is the first to look for and find a J-shaped relation between baseline BMI and weight gain in quitters. If confirmed, this has important implications for the treatment of tobacco addiction. Knowing that underweight and obesity predicts greater weight gain on cessation helps clinicians plan interventions with their patients and guides epidemiological and physiological investigations into causes of weight gain on smoking cessation.

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Table 2. Regression analysis for weight change over 8 years according to 4 groups of smoking status, smokers were used as the reference category

Smoking Status	Unadjusted regression coefficient	95%CI Lower	Upper	P value	R^2	Adjusted* regression coefficient	95%CI Lower	Upper	P value	R^2
Constant[#]	2.245	1.692	2.797		0.133					0.182
Abstainers	6.576	4.992	8.161	<0.001		6.810	5.232	8.389	<0.001	
Relapsed	1.047	-1.694	3.788	0.454		1.064	-1.655	3.783	0.442	
Late abstainers	6.108	4.722	7.494	<0.001		6.324	4.943	7.705	<0.001	

*Adjusted for confounding variables of baseline height, BMI, Horn-Russell Score, daily number of cigarettes, weekly units of alcohol, age in years, socioeconomic status and ethnic origin, gender and treatment group.
[#]In the unadjusted model, the constant can be interpreted as the weight gain in smokers (the reference group), but has no useful meaning in the adjusted model.

Table 3. Regression model for the effect of BMI on weight gain in abstainers

BMI terms	Unadjusted regression coefficient	95%CI Lower	Upper	P value	R^2	Adjusted* regression coefficient	95%CI Lower	Upper	P value	R^2
Constant	8.972	7.619	10.339							
BMI-linear#	0.382	0.008	0.757	0.045	0.047					
Constant	7.947	6.360	9.514							
BMI-linear#	0.177	-0.225	0.578			0.217	-0.175	0.609		
BMI-quadratic#	0.071	0.014	0.128	0.015	0.114	0.062	0.006	0.118	0.030	0.172

*Adjusted for confounding variables of baseline height, BMI, Horn Russell Score, daily number of cigarettes, weekly units of alcohol, age in years, socioeconomic status and ethnic origin. # Re-centred around the whole sample mean.

Table 4. Regression model for the effect of BMI on weight gain in smokers

1. Smoking Status	Unadjusted regression coefficient	95%CI Lower	Upper	P value	R^2	Adjusted* regression coefficient	95%CI Lower	Upper	P value	R^2
Constant	2.206	1.673	2.738		0.155					0.243
BMI[#]	-0.265	-0.401	-0.128	<0.001		-0.222	-0.358	-0.087	0.002	
Age in years[#]						-0.131	-0.186	-0.076	<0.001	

*Adjusted for confounding variables of baseline height, BMI, Horn Russell Score, daily number of cigarettes, weekly units of alcohol, age in years, socioeconomic status and ethnic origin. [#] Re-centred around the whole sample mean

Table 5. Estimated mean weight gain according to BMI for 'smokers', 'abstainers' and 'abstainers without potential outliers*', 'smokers combined with relapsers', and 'abstainers combined with late abstainers'

Baseline BMI	Mean weight (95% CI) gain estimated from regression models containing:						
	Smokers	Smokers Combined with relapsers	Abstainers	Abstainers excluding BMI>30kg/m^2	Abstainers excluding BMI >30kg/m^2 and weight gain >20kg	Abstainers combined with late abstainers	Abstainers combined with late abstainers excluding (BMI>40kg/m^2)
18	3.9 (2.9, 4.9)	4.0 (3.0, 5.1)	9.8 (6.1,13.5)	10.9 (6.4, 15.7)	10.3 (6.3, 14.4)	10.6 (7.9, 13.5)	11.9 (8.6, 14.7)
23	2.6 (2.0, 3.1)	2.7 (2.2, 3.3)	7.8 (6.4,9.3)	7.4 (5.6, 9.1)	7.2 (5.7, 8.9)	8.6 (7.5, 9.7)	8.4 (7.3, 9.6)
29	1.0 (0.2, 1.8)	1.1 (0.3, 1.8)	10.2 (7.9,12.5)	12.2 (5.7, 14.7)	10.2 (7.5, 16.8)	7.6 (6.2, 9.1)	7.6 (6.3, 8.8)
36	-0.8 (-2.4, 0.8)	-0.8 (-2.4, 0,7)	19.4 (12.7,26.0)			8.3 (7.2, 9.3)	11.2 (8.5, 13.9)
40	-2.6 (-5.1, -0.3)	-2.8 (-5.2, -0.3)				9.6 (7.8, 11.2)	

*outliers are BMI>30kg/m^2, weight gain >20kg and BMI>40kg/m^2

Figure 3. Predicted mean and confidence intervals for weight change according to BMI in smokers and abstainers.